

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-130. (Cancelled)

131. (New) A method for establishing whether at least one target polynucleotide is present in a sample, comprising the steps of

- i) adding, to a sample to be analysed for the presence of the at least one target polynucleotide, at least one polynucleotide probe at least partly complementary to a sub-sequence of the at least one target polynucleotide, wherein the at least one probe comprises at least one detectable label,
- ii) incubating the sample under conditions suitable for the formation of at least one hybrid polynucleotide comprising the at least one probe and the at least one target polynucleotide, when present,

- iii) recording spectral data from an environment comprising at least part of the sample,
- iv) analysing the spectral data using multivariate analysis, and
- v) establishing whether the target polynucleotide is present.

132. (New) The method according to claim 131, wherein the analysis of the spectral data can distinguish for each of the at least one probe whether the probe is part of the at least one hybrid polynucleotide or not part of the at least one hybrid polynucleotide.

133. (New) The method according to claim 131, wherein the analysis of the spectral data can distinguish for each of the at least one probe, when the probe is part of the at least one hybrid polynucleotide, whether or not there is a mismatch between the probe and the sub-sequence of the at least one target polynucleotide.

134. (New) The method according to claim 131, wherein the at least one probe has a length of 6 to 50 nucleotides.

135. (New) The method according to claim 134, wherein the sequence complementarity between target and probe in a range of overlap is at least 50%.

136. (New) The method according to claim 131, wherein one probe is capable of hybridising to two or more target polynucleotides.

137. (New) The method according to claim 131, comprising using at least two polynucleotide probes capable of hybridising to two different target polynucleotides.

138. (New) The method according to claim 131, comprising using at least two polynucleotide probes capable of hybridising to the same target polynucleotide.

139. (New) The method according to claim 131, wherein at least one probe comprises a probe selective for apolipoprotein B mutations related to atherosclerosis.

140. (New) The method according to claim 131, wherein at least one probe is selective for apolipoprotein E

polymorphism (apoE2, E3 and E4) related to neurological diseases.

141. (New) The method according to claim 131, wherein at least one probe is selective for human muscle glycogen synthase polymorphism related to diabetes mellitus.

142. (New) The method according to claim 131, wherein at least one probe is selective for methylene tetrahydrofolate reductase polymorphism related to osteoporose.

143. (New) The method according to claim 131, wherein at least one probe is selective for Dnasel mutations related to rheumatological diseases.

144. (New) The method according to claim 131, wherein at least one probe is selective for a mutation in the BRCA1 gene or in the BRCA2 gene.

145. (New) The method according to claim 131, wherein at least one probe is selective for mismatch repair gene mutations related to cancer.

146. (New) The method according to claim 131, wherein at least one target polynucleotide comprises RNA or DNA.

147. (New) The method according to claim 131, further comprising inclusion of various control polynucleotides in the hybridisation mixture, such as positive controls (wild-type, mutation, heterozygote), negative control (dummy DNA sequence).

148. (New) The method according to claim 131, wherein at least one target polynucleotide has a length of 8 bases to 1000 kb.

149. (New) The method according to claim 131, wherein the length of the overlap between the probe and target polynucleotide is at least 5 nucleotides.

150. (New) The method according to claim 131, wherein the length of at least one probe is 7 to 1000 nucleotides.

151. (New) The method according to claim 131, wherein the nucleotide being complementary to a polymorphism/mutation in a target polynucleotide is positioned in the 3' or 5' terminal of the probe.

152. (New) The method according to claim 131, wherein  
the nucleotide being complementary to a  
polymorphism/mutation in a target polynucleotide is  
positioned in the centre of the probe.

153. (New) The method according to claim 131, wherein  
the probe comprises a sequence which is complementary to the  
sequence lying immediately upstream or immediately  
downstream to a polymorphic site in the target  
polynucleotide and the probe does not contain a nucleotide  
being complementary to the polymorphic site.

154. (New) The method according to claim 131, wherein at  
least one label is bound to the 3' or 5' terminal nucleotide  
of the probe.

155. (New) The method according to claim 131, wherein at  
least one label is bound to a non-terminal nucleotide of the  
probe.

156. (New) The method according to claim 131, wherein at  
least one label is bound to the nucleotide being  
complementary to the polymorphic site.

157. (New) The method according to claim 131, wherein at least one label is bound to a nucleotide at least 1 nucleotide upstream or downstream to the nucleotide complementary to the polymorphic site.

158. (New) The method according to claim 131, wherein at least one probe has at least two stretches of complementarity to at least one target polynucleotide.

159. (New) The method according to claim 158, wherein two stretches are separated by a nucleotide sequence, which does not hybridise to the target polynucleotide.

160. (New) The method according to claim 131, further comprising amplification of a polynucleotide prior to hybridisation.

161. (New) The method according to claim 131, wherein undesired hybridisation reactions are prevented by the addition of one or more helper polynucleotides capable of hybridising to the target polynucleotide at a sub-sequence which does not overlap with the sub-sequence to which the probe hybridises.

162. (New) The method according to claim 131, wherein prior to the hybridisation, a step aimed at generating single stranded polynucleotides is performed.

163. (New) The method according to claim 131, wherein the formation of a hybrid polynucleotide takes place under conditions of

- a) optimal or suboptimal stringency providing sufficient stable complexes for discriminatory signal detection,
- b) any composition of buffers optimising discriminatory signal detection,
- c) any form and concentrations of one or more salts optimising discriminatory signal detection,
- d) any additives including but not limited to stabilisers and/or quenchers optimising discriminatory signal detection,
- e) temperature range for hybridisation specific for any specific combination of analyte and probe optimising discriminatory signal detection, and/or
- f) any range of time of hybridisation necessary to optimise discriminatory signal detection.

164. (New) The method according to claim 131, wherein hybridisation is carried out under conditions of high stringency allowing hybridisation only between perfect matches.

165. (New) The method according to claim 131, wherein hybridisation is carried out under conditions of medium to high stringency allowing hybridisation between probe and target in the presence of one or more mismatches.

166. (New) The method according to claim 131, wherein hybridisation is carried out in solution.

167. (New) The method according to claim 131, wherein the target or the probe is linked to a solid support prior to hybridisation.

168. (New) The method according to claim 131, wherein at least one probe hybridises only to one target polynucleotide.

169. (New) The method according to claim 131, wherein at least one probe hybridises to both a wild-type target

polynucleotide and to a target polynucleotide carrying a mutation or polymorphism.

170. (New) The method according to claim 131, wherein recording spectral data comprises detection of signal for at least 10 discrete wavelengths.

171. (New) The method according to claim 170, wherein the distance between the discrete wavelengths is 10 nm or less.

172. (New) The method according to claim 131, wherein the spectral data recorded comprises a fluorescence spectrum between 180 and 950 nm.

173. (New) The method according to claim 131, further comprising recording of spectral data from the polynucleotide probe alone.

174. (New) The method according to claim 131, further comprising recording spectral data from the hybrid polynucleotide and from a polynucleotide probe alone and/or, from a non-hybridising polynucleotide probe contacted by the

target polynucleotide, and/or from a polynucleotide probe contacted with a non-hybridising polynucleotide sequence.

175. (New) The method according to claim 131, wherein multivariate analysis comprises general multivariate analysis, principal component analysis and extensions of this, exploratory and confirmatory factor analysis in its various forms, Cluster and latent class analysis including scaled latent class analysis, structural equation analysis, Fixed mixture analysis and combinations hereof.

176. (New) The method according to claim 131, wherein the spectral data are recorded via mass spectroscopy.

177. The method according to claim 131, further comprising the step of determining the presence or absence of a mutation or polymorphism in the genome of an individual on the basis of the information obtained concerning the presence or absence of the at least one target polynucleotide.

178. (New) The method according to claim 131, further comprising the step of diagnosing a disease or health related state or determining a genetic predisposition of an

individual on the basis of the information obtained concerning the presence or absence of the at least one target polynucleotide.

179. (New) A kit for detection of a mutation or a polymorphism comprising

at least one oligonucleotide probe capable of hybridising to a preselected region of a target polynucleotide, the polynucleotide probe further comprising at least one detectable label,

instructions enabling correlation of spectral data recorded from a hybrid polynucleotide between said at least one oligonucleotide probe and said target polynucleotide to the presence or absence of said mutation or polymorphism using multivariate analysis.

180. (New) The kit according to claim 179, further comprising at least one control polynucleotide capable of hybridising to the oligonucleotide probe and non-hybridising polynucleotide(s)

181. (New) A system for establishing whether at least one target polynucleotide is present in a sample, comprising

- i) at least one polynucleotide probe being at least complementary to a target polynucleotide, the probe comprising a detectable label,
- ii) a sample chamber from which electromagnetic radiation can be recorded,
- iii) a source of spectrally resolved electromagnetic radiation,
- iv) means for sensing and recording a spectrum of electromagnetic radiation from the sample chamber, and
- v) a computer unit for storing spectral data of electromagnetic radiation and having instructions to treat the recorded spectral data using multivariate analysis.

182. (New) A system for detection of a hybrid polynucleotide comprising

- i) at least one oligonucleotide probe being at least partly complementary to a target polynucleotide, the probe comprising a detectable label,
- ii) a sample chamber from which electromagnetic radiation can be recorded,

- iii) a source of spectrally resolved electromagnetic radiation,
- iv) means for sensing and recording a spectrum of electromagnetic radiation from the sample chamber, and
- v) a computer unit for storing spectral data of electromagnetic radiation and having instructions to treat the recorded spectral data using multivariate analysis.